Pushing back boundaries with ultra-low volume pipetting

The Novartis Animal Health Research Center has invested in an automated compound logistics system to aid drug discovery, taking advantage of the exceptional pipetting capabilities of the MultiChannel Arm[™] 384.





Vincent Beuret with the Center's Freedom EVO system

"We can pipette down to o.1 μl of compound with a CV of 10 %, which is impressive." The Novartis Animal Health Research Center in Saint-Aubin, Switzerland, is engaged in developing anti-parasitic and therapeutic products for veterinary use. The Company has automated picking, distribution and dissolution of compounds on a Freedom EVO[®] system, enabling the pre-discovery screening group to benefit from the extremely low volume pipetting offered by the MultiChannel Arm 384 (MCA 384). Scientist Vincent Beuret explained: "Our group screens potential candidates against a range of parasites, such as filarial and gastric parasites, fleas, ticks and flies, and tests hundreds of thousands of compounds a year. The initial in vitro testing allows us to determine whether a compound is active on a particular parasite, and to get an indication of the dose that is required. We can then pre-select suitable candidates to undergo further studies to establish the activity and toxicity in vivo. To help with this work, a new automated compound logistics system was installed last year. A Freedom EVO 150 platform with an eight-channel Liquid Handling (LiHa) Arm is linked to a customized LiCONic StoreX Kiwi TubeStore. A Te-Link™ module connects the

Freedom EVO 150 to a second liquid handling platform, a Freedom EVO 200 equipped with an MCA 384, allowing plates to be transferred between the workstations. Each Freedom EVO platform is controlled independently by Tecan's Freedom EVOware® software, which gives us the option to use either platform in isolation if necessary."

"Mother solutions – 10 mg/ml or 10,000 ppm solutions in DMSO of all the compounds that we are interested in – are pre-selected for screening tests. The chosen mother solutions are stored in the Kiwi unit until needed, then transferred to the Freedom EVO 150, where the LiHa prepares 96-well daughter plates containing suitable dilutions of these compounds. The Te-Link module moves the daughter plates across to the Freedom EVO 200, where the MCA 384 allows us to generate 96- and 384-well test plates, according to the size of the parasite. This is an important stage, as we are often pipetting extremely small volumes of compound; we can pipette down to 0.1 µl of compound with a CV of 10 %, which is impressive."

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Vincent continued: "I attended a Tecan training course for the MCA, and this helped me to establish the best parameters for different liquid classes and find the ideal settings for reproducible, accurate pipetting."



The Novartis team has achieved reliable pipetting down to 0.1 μl using the MCA 384

"The lastest edition of the Freedom EVOware is also a real step forward for us." "To perform such low volume pipetting, we initially draw up 4.9 µl of media, followed by 0.1 µl of compound, and then dispense the entire 5 µl volume so that the media flushes the entire compound from the tip. We noticed differences in the results depending on the media used, and optimized our procedures to account for this. We discovered that optimal pipetting quality is achieved when water containing a small percentage (0.05 %) of Tween 20 is used. This also promotes greater interaction between the candidate compounds and the parasite, further enhancing assay performance."

"We were able to move from our old Tecan system directly to the new platform without a break in our screening investigations. As the LiHa handles the largest volumes of mother solution, which is where there is the greatest risk of contamination, its liquid displacement pipetting system is important, giving us the capability to thoroughly flush the system. The MCA 384 was chosen for its flexibility; although we use 96-well daughter plates at the moment, with the MCA we have the option to move to 384-well plates in the future. This would save time, as we could transfer compounds from daughter plates to 384-well test plates in one procedure, rather than the current four-step protocol. The latest edition of Freedom EVOware is also a real step forward for us; it is very robust, and we can certainly see the benefits of 10 years of development."

Vincent concluded: "We receive good support from Tecan, and are very happy with the implementation of the compound logistics system, as well as how the project has progressed; it is always nice when you find something that works well, and that lasts a long time without the need for constant modifications. It is really nice to know that your work is going to last."

To find out more on Tecan's MCA 384, visit **www.tecan.com/mca384**

To find out more about Novartis Animal Health, visit **www.ah.novartis.com**